Risk Assessment Summary

for

NSN-18967: *Saccharomyces* species yMHCT484

(Manufacture and export for use in bioethanol production)

Introduction

Under the *Canadian Environmental Protection Act, 1999* (CEPA), animate products of biotechnology (i.e. “living organisms”) not listed on the Domestic Substances List (DSL) are considered “new” to Canada. Information and data prescribed by the *New Substances Notification Regulations (Organisms)* [NSNR(O)] must be submitted before they are manufactured or imported, and Environment and Climate Change Canada (ECCC) and Health Canada (HC) must assess their potential to harm human health and the environment.

Saccharomyces species yMHCT484, a yeast that was proposed to be manufactured in Canada for export to the United States (for use in the production of ethanol), was assessed according to the requirements for Schedule 2 of the NSNR(O), which applies to new living organisms that are not intended for introduction outside a contained facility or for export only. Living organisms notified under this schedule are not eligible for addition to the DSL.

Regulatory Decision

Based on the assessment described below, manufacture of *Saccharomyces* species yMHCT484 within a contained facility for export is not considered to be harmful to human health or the environment. In addition, *Saccharomyces* species yMHCT484 is not entering the environment in a quantity or under conditions that pose a danger to the environment or humans. Therefore no further action is recommended as a result of this assessment.

After December 1, 2016, the manufacture of *Saccharomyces* species yMHCT484 could proceed in Canada.

Background

Saccharomyces species yMHCT484 is a yeast that was genetically modified to produce the glucoamylase enzyme, leading to higher ethanol yields.

Hazard Considerations

With respect to the environment
The environmental hazard potential of *Saccharomyces* species yMHCT484 is considered to be medium for the following reasons:

- Very little is known about the specific growth conditions of *Saccharomyces* species yMHCT484. However the species to which *Saccharomyces* species yMHCT484 belongs to has been isolated from different environments with varying ecological conditions and is known to be able to survive under starvation conditions.
- The toxicity and pathogenicity potential of *Saccharomyces* species yMHCT484 and its parental strain have not been tested. However, various strains from the the species to which *Saccharomyces* species yMHCT484 belongs to have been reported to cause disease in terrestrial vertebrates and invertebrates as well as in aquatic invertebrates. Considering the long history of industrial use with this species, the number of reported adverse effects is relatively small.
- Given that the source of the introduced genetic material to *Saccharomyces* species yMHCT484 is a wood degrading fungus, it is not known if the notified organism would be pathogenic to plants or not.

With respect to human health
The human hazard potential of *Saccharomyces* species yMHCT484 is considered to be medium for the following reasons:

- Cases of allergic reaction involving the species to which *Saccharomyces* species yMHCT484 belongs have been reported. However those cases were usually related to repeated and prolonged occupational exposures. In the case of *Saccharomyces* species yMHCT484, the genetic modifications may also increase the potential of the micro-organism to cause allergic reactions in some individuals following exposure.
    - Although there are reported cases of adverse human health effects related to the species to which *Saccharomyces* species yMHCT484 belongs, the majority of these cases involve individuals with compromised immunity or with underlying diseases or medical conditions.

- As *Saccharomyces* species yMHCT484 is susceptible to 5-flucytosine, caspofungin, voriconazole and itraconazole, in the unlikely event of an infection with the notified strain, clinically relevant antifungals are available for treatment.

The following considerations were also taken into account in the assessment of human health and environmental hazard:

- *Saccharomyces* species yMHCT484 has been accurately identified.
- The introduced genetic elements in *Saccharomyces* species yMHCT484 are well characterized and are considered stable.
- The parental strain from which *Saccharomyces* species yMHCT484 has been derived does not have a history of use as a production organism in Canada. However, the species to which *Saccharomyces* species yMHCT484 belongs has a long history of safe use in industrial applications.

Exposure Considerations

With respect to the environment and humans
The environmental and human exposure potential from manufacture of *Saccharomyces* species yMHCT484 for export is considered to be low for the following reasons:

- *Saccharomyces* species yMHCT484 is manufactured solely in a contained facility at a single location in Canada, to be exported to the United States. The manufacturing process meets, at a minimum, the standards for the Biosafety Level 1 - Large Scale requirements, as defined in Appendix K of the 2016 National Institutes of Health (NIH) Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules.
- Manufacture is in a closed system. All wastes containing *Saccharomyces* species yMHCT484 will be adequately treated and inactivated prior to disposal or release of the waste. As a result, the potential for release into the environment of viable organisms and the introduced genetic material is low.
- The operations will be undertaken by trained personnel, and appropriate SOPs, including emergency procedures, are in place to deal with any spills and accidental releases. As a result, no significant releases are expected that may lead to exposure of bystanders and the general population.
- The species to which the notified micro-organism belongs has the ability to grow in different environments under varying ecological conditions and is able to

survive, persist and disseminate in nature in the form of ascospores when growing conditions are not optimal.

Risk assessment conclusion

Risk is typically described as the probability of an adverse effect occurring based on hazards and a particular scenario of exposure (Environment Canada and Health Canada, 2011). Exposure scenarios can be described based on intended and any potential uses. In the present case, *Saccharomyces* species yMHCT484 will be manufactured in Canada for export to the United States where it will be used for industrial production of ethanol. No other uses for the substance are envisaged.

With respect to the environment (for manufacture and export)
While *Saccharomyces* species yMHCT484 was assigned a medium potential environmental hazard, given the low potential environmental exposure, the environmental risk associated with the manufacture of *Saccharomyces* species yMHCT484 is assessed to be low.

With respect to human health (for manufacture and export)
While *Saccharomyces* species yMHCT484 was assigned a medium potential human health hazard to the general population, given the low potential human exposure, the human health risk associated with the manufacture of *Saccharomyces* species yMHCT484 is assessed to be low.

References

(excluding proprietary information or references provided by the notifier)

NIH Guidelines (2016). NIH guideline for research involving recombinant or synthetic nucleic acids molecules. https://osp.od.nih.gov/wp-content/uploads/2013/06/NIH_Guidelines.pdf (viewed 16 July 2018).

Environment Canada and Health Canada (2011). Framework for Science-Based Risk Assessment of Micro-Organisms Regulated under the Canadian Environmental Protection Act, 1999 (2011). http://www.ec.gc.ca/subsnouvelles-newsubs/default.asp?lang=En&n=120842D5_1 (viewed May, 2018).